REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 1, 2 and 4 were pending in this application when last examined and stand rejected. In order to expedite allowance, claim 2 is canceled without prejudice or disclaimer thereto.

II. CLAIM OBJECTION

On pages 2 and 3 of the Office Action, claim 2 was objected to as being improperly dependent for failing to further limit the subject matter of the claim upon which it depends. This claim is canceled in order to expedite allowance, and therefore this objection is moot.

III. ANTICIPATION REJECTION

In item 10 on pages 3 and 4 of the Office Action, claims 1, 2 and 4 were again rejected under 35 U.S.C. § 102(b) as anticipated by Wolinsky et al. Applicants respectfully traverse this rejection as applied to the remaining claims.

Applicants note that claim 1 is directed toward a method for quantitatively analyzing specimen molecules comprising (1) passing a solution containing the specimen molecules and a solution containing fluorescent probe molecules capable of complexing with the specimen molecules through a micro flow channel to form a laminar flow; (2) selectively promoting diffusion of the complex formed by the fluorescent probe molecules and the specimen molecules in the laminar flow; and (3) fluorometrically determining the degree of diffusion of the complex formed between the specimen molecules and the probe molecules within the micro flow channel by detecting fluorescent signals and comparing the results to a predetermined calibration curve.

Applicants further note that claim 4 is drawn to a similar method utilizing DNA fragments and a probe capable of forming a complex to the DNA complex.

The Office indicates that the method taught in Wolinsky et al. anticipates each and every element of these claims. However, the two steps as disclosed in the sentences running from page

12 to page 13 of Wolinsky et al. (solution hybridization and flow cytometric analysis) are not identical with the analytical methods disclosed in claims 1 and 4 of the present invention.

In particular, in the method of Wolinsky et al., cells are complexed in the hybridization step, where a preparatory stage of the analysis is carried out, and then the actual analysis is performed by flow cytometry. In other words, Wolinsky et al. teaches combining cells and probes and then performing such analysis on the combined cells and probes.

On the other hand, in the present invention, the steps from the formation of a complex to analysis are performed only during passing solutions through a micro flow channel. Thus, as shown in step (1) of claims 1 and 4, at least two solutions, one containing the specimen molecules and another containing the probe molecules, are passed through a micro flow channel. Wolinsky et al., as indicated above, passes a single solution containing the hybridized cells through flow cytometry.

Thus, Applicants note that the claimed invention is not taught by Wolinsky et al.

Further, the flow cytometric analysis of Wolinsky et al. and the analytical method of the present invention are quite different. In step (1) of the present invention, it is indispensable to form a laminar flow in the micro flow channel. On the other hand, a particulate dispersion, a particle in which is used as a solid-phase carrier, is allowed to pass through a fine flow channel in the cytometric analysis of Wolinsky et al., but there is no utilization of any fluid dynamic characteristics capable of forming a laminar flow as required in the present invention. In case of the method of Wolinsky et al., a turbulent flow of the dispersion is more effective than a laminar flow. Next, in the step (2) of the present invention, the complex is selectively brought into diffusion. In contrast, no change is formed in diffusion coefficient in the cytometric analysis of Wolinsky et al. wherein particles as a solid carrier are dispersed into a solution to prepare a dispersed solution. Finally, in the step (3) of the present invention, analysis is carried out by detecting the degree of diffusion of the complex and comparing the result to a predetermined calibration curve. In the cytometric analysis of Wolinsky et al., however, no change is formed in the diffusion coefficient so that analysis utilizing the degree of diffusion cannot be carried out in Wolinsky et al.

Thus, Applicants again note that Wolinsky et al. fails to teach or suggest the claimed invention.

Furthermore, Applicants note that on page 6 of the Office Action, the Office contended that the specification does not set forth a limiting definition of "selectively promoting diffusion". However, Applicants note that on pages 6 and 7, paragraph [0034], of the specification, it is taught that diffusion can be selectively accelerated of the complex as formed. In other words, selective diffusion is diffusion caused by affinity between the probe and specimen molecules in addition to conventional diffusion. Applicants note such is not taught by Wolinsky et al.

The Office also argues that Wolinsky et al. teaches analysis of the degree of diffusion by reference to a calibration curve (page 4, lines 2-3), i.e. a standard curve of Wolinsky et al. corresponds to the calibration curve used in the present invention. However, the standard curve of Wolinsky et al. is used for calibration of instruments, which is categorically different from the calibration curve of the present invention used for quantitative analysis. It is usual practice to calibrate instruments prior to analyzing a substance. Thus, a person skilled in the art would not deem calibration of instruments equivalent to quantitative analysis. Further, the calibration curve of the present invention cannot be employed for calibration of instruments.

Thus, for the above-noted reasons, Applicants suggest this rejection is untenable and should be withdrawn.

IV. OBVIOUSNESS REJECTION

On pages 5 and 6 of the Office Action, claims 1, 2 and 4 were again rejected under 35 U.S.C. § 103(a) as obvious over Wolinsky et al. in view of Chee et al. Applicants respectfully traverse this rejection as applied to the remaining claims.

In particular, the Office alleges that the skilled artisan would have been motivated to combine the teachings of Wolinsky and Chee because Chee teaches comparing analyte data to calibration curves allows the artisan to determine the amount of analyte present, and that the combination of Chee and Wolinsky would result in a method of quantitation of a target analyte in a sample by use of a calibration curve (page 6, lines 10-15, of the Office Action). In other words, the Office contends that the analytical method of the present invention is easily inferred from a combination of Chee et al. wherein the art of quantitatively analyzing samples by using a calibration curve is disclosed and Wolinsky et al. wherein the cytometric analysis and standard curve are disclosed.

As noted above, however, Wolinsky et al. uses a standard curve for calibration of instruments. Also, Wolinsky et al. fails to teach utilization of selective diffusion in a micro flow channel to quantitatively analyze specimen molecules.

Furthermore, Applicants note that a skilled artisan could not merely combine the teachings of these two references to arrive at the claimed invention. In particular, Wolinsky et al. teaches preincubation of the cells and the probe, followed by flow cytometry. The Office contends Chee is directed toward comparing analyte data to calibration curves to determine the amount of analytes present. However, the present invention uses a calibration curve to indicate the amount of specimen molecule based on the degree of diffusion within the micro flow channel. The combination of the cited references does not instruct a person of skill in the art to use a calibration curve to correlate the amount of diffusion in the micro flow channel.

Further, as in the case of Wolinsky et al., Chee et al. also utilizes a method wherein particles of solid-phase carriers are dispersed into a solution and the resultant dispersed solution is allowed to pass through a flow channel to analyze the individual particles. Additionally, it is necessary to fix complex-forming molecules on the particles in Chee et al. In a method of fixing the molecules on a solid phase carrier through the particles, a high density array is formed conveniently in Chee et al. Thus, Chee et al. is different from the present invention wherein the operations from the formation of a complex to the analysis are performed only by passing the solutions through micro flow channels. Thus, the analytic method of the present invention is not rendered obvious by combining the teachings of quantitation by calibration curve disclosed in Chee et al. and the analytical method of Wolinsky et al.

Finally, the analytical method of the present invention is aimed, as described in the Background Technology of the present specification, at achieving high precision not obtained hitherto by analytical methods utilizing PCR reaction, as taught in Wolinsky et al. Further, the present invention was developed to overcome drawbacks such as non-uniformity in the efficiency of immobilization of the probe molecules, poor reproducibility, and complexity in analysis in analytical methods wherein a probe molecule is immobilized, as taught in Chee et al. In addition, accomplishment of analysis was only by passing the solutions simply through the micro flow channel without carrying out technically difficult hybridization prior to analysis, as described in the paragraph [0030] of the present specification, is not easily thought out, even by a

combination of Wolinsky et al. and Chee et al., because both these references require hybridization. In particular, Chee et al. has to repeat the hybridization operations several times.

Thus, Applicants note that Wolinsky et al. in view of Chee et al. fails to teach or suggest each and every element of the claimed invention.

V. DOUBLE PATENTING REJECTION

In item 15 on pages 7-10 of the Office Action, claims 1 and 4 were newly provisionally rejected on the grounds of nonstatutory obviousness-double patenting over claims 1 and 3 of copending application No. 10/527,987 in further view of Chee et al.

Applicants will abandon copending application No. 10/527,987 to expedite allowance of this case, thereby rendering this rejection moot.

VI. CONCLUSION

In view of the foregoing amendments and remarks, the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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